4504 *J. Org. Chem.* **1996,** *61,* 4504−4505

A Novel Fluorine-Containing [2]Catenane

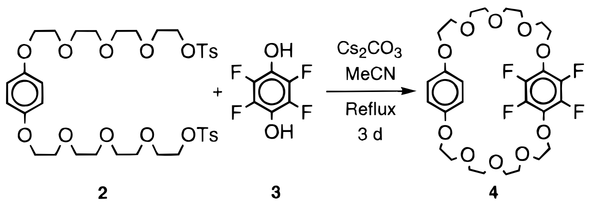
Richard E. Gillard,† J. Fraser Stoddart,*,†
Andrew J. P. White,‡ Brian J. Williams,§ and
David J. Williams‡

School of Chemistry, University of Birmingham,
Edgebaston, Birmingham B15 2TT, U.K., Department of
Chemistry, Imperial College, South Kensington,
London SW7 2AY, U.K., and Merck Sharp & Dohme
Research Laboratories, Neuroscience Research Centre,
Terlings Park, Harlow CM20 2QR, U.K.

Received March 20, 1996 (Revised Manuscript Received May 16, 1996)

Aryl−aryl interactions[1] have been shown to be important in the self-assembly[2] of [n]catenanes,[3] such as the [2]catenane **1**·4PF$_6$[4] constructed by us[5] back in 1989. Moreover, these interactions appear to have a strong influence upon the yields obtained in the template-directed[6] synthesis of the catenanes and upon the dynamic processes occurring within their molecular frameworks. Investigations have so far focused on changing the π-electron acceptor properties of the tetracationic cyclophane[7] and the π-electron donor properties of the neutral component.[8] In the present investigation, we have sought to reduce the π-electron-donating nature of the hydroquinone rings in the bis-*p*-phenylene-34-crown-10 component by incorporation of electron-withdrawing substituents into the hydroquinone rings. In this regard, fluorine atom substituents are interesting on account of their size complementarity with hydrogen ($r_F = 1.35$ Å, $r_H = 1.10$ Å), combined with their drastically different electronic properties. The physical and chemical properties of aromatic fluorine compounds[9] are dominated by the powerful negative inductive effect of the fluorine atoms and by the donation of electron density from the *p*-electrons of fluorine into the π-system of the aromatic ring. Modification of the structures of biologically-important molecules by fluorine substitution is well known.[10] However, examples in the literature of fluorine being employed to influence aryl−aryl interactions in supramolecular[11] and related systems are limited.[12−14]

Scheme 1



In this paper, we report (i) the synthesis and solid-state structure of *p*-phenylenetetrafluoro-*p*-phenylene-34-crown-10 (**4**), (ii) the self-assembly and solid-state structure of the [2]catenane **7**·4PF$_6$ incorporating **4** and cyclobis(paraquat-*p*-phenylene), and (iii) variable-temperature ^{1}H NMR spectroscopic studies carried out on **7**·4PF$_6$. The macrocyclic polyether **4** was synthesized as shown in Scheme 1. The bistosylate **2** was reacted with tetrafluorohydroquinone (**3**) in the presence of Cs$_2$CO$_3$ to give the macrocyclic polyether **4** in 14% yield.

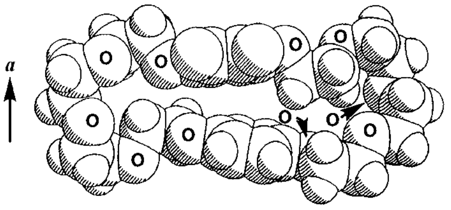


Figure 1. Space-filling representation of **4** in the solid state.

The X-ray structural analysis of **4**[22] shows (Figure 1) that the macrocycle is self-filling, with the hydroquinone ring and its tetrafluoro counterpart in proximal (centroid−centroid separation, 4.27 Å) overlapping, but with slightly tilted (angle between their mean planes, 16°) relative orientations. The planarity of the hydroquinone ring extends to include its adjacent *anti*-disposed OCH$_2$CH$_2$ units,[15] but for the tetrafluoro-*p*-phenylene ring, this geometry is, not surprisingly, different with the two OCH$_2$CH$_2$ units orientated approximately orthogonally with torsional twists about the −OC$_6$F$_4$O− bonds of 80 and 81°. The macrocycles pack to form continuous polar

---

† University of Birmingham.

‡ Imperial College London.

§ Merck Sharp & Dohme.

(1) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768−4774. Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525−5534. Hunter, C. A. *Chem. Soc. Rev.* **1994**, *23*, 101−109. Nishio, M.; Umezawa, Y.; Hirota, M.; Takeuchi, Y. *Tetrahedron* **1995**, *51*, 8665−8701.

(2) Lindsey, J. S. *New J. Chem.* **1991**, *15*, 153−180. Philp, D.; Stoddart, J. F. *Synlett* **1991**, 445−458. Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science* **1991**, *254*, 1312−1319. Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D. M. *Acc. Chem. Res.* **1995**, *28*, 37−44. Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1154−1196.

(3) Schill, G. In *Catenanes, Rotaxanes and Knots*; Academic Press: New York, 1971. Walba, D. M. *Tetrahedron* **1985**, *41*, 3161−3212. Sauvage, J. P. *Acc. Chem. Res.* **1990**, *23*, 319−327. Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2828.

(4) **1**·4PF$_6$ is the analog of **7**·4PF$_6$ in Scheme 2, where the four F atoms on the tetrafluoro-*p*-phenylene ring are replaced by H atoms.

(5) Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodnow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewicz, M.; Prodi, L.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 193−218.

(6) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res.* **1993**, *26*, 469−475. Hoss, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 375−384.

(7) Ashton, P. R.; Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M. T.; Menzer, S.; Pérez-García, L.; Prodi, L.; Stoddart, J. F.; Venturi, M.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1995**, *117*, 11171−11197.

(8) Amabilino, D. B.; Ashton, P. R.; Brown, C. L.; Córdova, E.; Godínez, L. A.; Goodnow, T. T.; Kaifer, A. E.; Newton, S. P.; Pietraszkiewicz, M.; Philp, D.; Raymo, F. M.; Reder, A. S.; Rutland, M. T; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1995**, *117*, 1271−1293 and references therein.

(9) Pavlath, A. E.; Leffler, A. J. *Aromatic Fluorine Compounds*; ACS Monograph Series No. 155; Reinhold Publishing Corporation: London, 1961. Tatlow, J. C. *Endeavour* **1963**, *22*, 89−95. Sheppard, W. A. *J. Am. Chem. Soc.* **1970**, *92*, 5419−5422. Chambers, R. D. In *Chemistry of Organic Fluorine Compounds*, 2nd ed.; Wiley: New York, 1976. Hunter, C. A.; Kapteijn, G. M.; Koten, G.; Lu, X-J. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 2009−2015.

(10) Schlosser, M. *Tetrahedron* **1978**, *34*, 3−17. Gerstenberger, M. R. C.; Haas, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 647−664. Welch, J. T. In *The Effects of Selective Fluorination on Reactivity in Organic and Bioorganic Chemistry*; Welch, J. T., Ed.; ACS Symposium Series No. 456; American Chemical Society: Washington, DC, 1991; pp 1−15.

(11) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89−112. Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1009−1020. Pedersen, C. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1021−1027. Lehn, J.-M. In *Supramolecular Chemistry—Concepts and Perspectives*; VCH: Weinheim, 1995.

(12) Patrick, C. R.; Prosser, G. S. *Nature (London)* **1960**, *187*, 1021. Williams, J. H.; Cockcroft, J. K.; Fitch, A. N. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1655−1657.

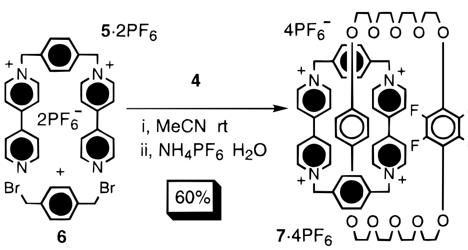
(13) Laatikainen, R.; Ratilainen, J.; Sebastian, R.; Santa, H. *J. Am. Chem. Soc.* **1995**, *117*, 11006−11010.

(14) Cozzi, F.; Ponzini, F.; Annunziata, R.; Cinquini, M.; Siegel, J. S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1019−1020 and references therein.

(15) Makriyannis, A.; Fesik, S. *J. Am. Chem. Soc.* **1982**, *104*, 6462−6463.

S0022-3263(96)00533-6 CCC: $12.00

Scheme 2



stacks that extend in the crystallographic *a* direction. The centroid−centroid separation between the hydroquinone ring in one macrocycle and its tetrafluoro counterpart in the next macrocycle is 4.11 Å. As the molecules crystallize in a noncentrosymmetric space group, stacks of one polarity only are present in a given crystal.

The [2]catenane **7**·4PF$_6$ was self-assembled (Scheme 2) by reacting the macrocyclic polyether **4** with the salt **5**·2PF$_6$ and 1,4-bis(bromomethyl)benzene (**6**) in MeCN at ambient temperature and pressure. The [2]catenane **7**·4PF$_6$ was isolated as a red solid in 60% yield after column chromatography and counterion exchange.

Dynamic processes occurring in the [2]catenane **7**·4PF$_6$ in the solution state (CD$_3$CN and CD$_3$COCD$_3$) were investigated by variable-temperature ^{1}H NMR spectroscopy (400 MHz). In solution, *only one translational isomer* could be observed—*i.e.*, the one in which the hydroquinone ring is located inside the cavity of the tetracationic cyclophane.[16] Below 235 K, the appearance of two resonances for the *p*-phenylene protons in the tetracationic cyclophane is in accordance with the circumrotation of the tetracationic cyclophane through the cavity of the macrocyclic polyether component[17] being slow on the ^{1}H NMR time scale. This process almost certainly involves the disruption of any interaction between the alongside hydroquinone ring and the bipyridinium unit of the tetracationic cyclophane. The free energy of activation ($\Delta G^{\ddagger}$) for this process was calculated[18] to be 11.4 kcal mol^{-1}.

The X-ray crystal structure (Figure 2) of the [2]catenane **7**·4PF$_6$[22] shows that the hydroquinone ring of the macrocyclic polyether is positioned within the cavity (−OC$_6$H$_4$O− axis inclined by 47° to the mean plane of the tetracationic cyclophane) of the tetracationic cyclophane, while the tetrafluoro counterpart lies on the outside.[19] A noticeable feature of the outside positioning of the tetrafluoro-*p*-phenylene ring is its distinctly tilted orientation with respect to the inside bipyridinium unit, a conformational arrangement present also in the free macrocycle. The inside hydroquinone ring is almost exactly centrally-located within the tetracationic cyclophane,[20] which has a length and breadth of 10.23 and 6.98 Å, respectively. The mean interplanar separations between the hydroquinone ring and the inside and outside bipyridinium units are 3.47 and 3.50 Å, respectively. In addition to the $\pi-\pi$ stabilizing interactions between these residues, there are both edge-to-face CH···π (H···π, 2.87 Å, C−H···ring centroid angle, 160°) interactions between hydroquinone CH hydrogen atoms and *p*-phenylene rings of the tetracationic cyclophane and C−H···O (C···O, 3.29, 3.29 Å, H···O, 2.41, 2.45 Å, C−H···O angle, 153, 146°) hydrogen bonds between bipyridinium protons and the central oxygen of each polyether linkage. In contrast to **1**·4PF$_6$, where continuous donor/acceptor stacks are formed in the crystals, here discrete centrosymmetrically related "dimer-pairs"[21] are formed wherein the tetrafluoro-*p*-phenylene rings are in a parallel overlapping arrangement with a ring−ring interplanar separation of 3.21 Å and an associated centroid−centroid distance of 3.89 Å.

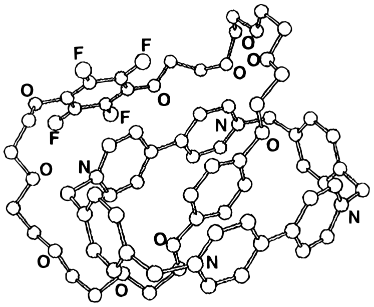


Figure 2. Ball-and-stick representation of the solid state structure of the [2]catenane **7**·4PF$_6$.

In the knowledge that the tetrafluorohydroquinone ring shows no propensity for inclusion within the cavity of the tetracationic cyclophane, it is remarkable to note that the self-assembly of the [2]catenane **7**·4PF$_6$ proceeds in such high (60%) yield (*cf.* 70% for the self-assembly of **1**·4PF$_6$). This decrease in yield is small considering that one of the recognition sites has effectively been "switched off".

Incorporation of fluorine atoms into organic compounds has led to a tremendous number of materials with novel and exciting properties. We hope to employ further the unique chemistry of fluorine, not only to influence the molecular recognition in self-assembled molecular compounds, but also to increase fundamental understanding[14] of interactions between aromatic units.

Acknowledgment. This research was supported by the Engineering and Physical Sciences Research Council as well as by Merck Sharp & Dohme in the U.K.

Supporting Information Available: Experimental procedures and characterization data (3 pages).

JO960533J

---

[16] This observation is in accordance with ^{1}H and ^{19}F NMR spectroscopic studies involving 1,4-bis(2-(2-hydroxyethoxy)ethoxy)-tetrafluorobenzene and cyclobis(paraquat-*p*-phenylene) in CD$_3$CN at 25 °C, which indicated that no complex formation occurs.

[17] For a full discussion of the dynamic processes occurring within the [2]catenane molecular architecture, see ref 4.

[18] The kinetic data were obtained by the coalescence method, where values of the rate constant (k_c) at the coalescence temperature (T_c) were obtained (Sutherland, I. O. *Annu. Rep. NMR Spectrosc.* **1971**, *4*, 71−235) from the approximate expression, $k_c = \pi(\Delta\nu)/(2)^{1/2}$, where $\Delta\nu$ is the limiting chemical shift difference (in hertz) between the exchanging proton resonances. The Eyring equation was then used to calculate $\Delta G^{\ddagger}{}_c$.

[19] Computational studies, using both molecular mechanics and semiempirical quantum mechanical methods, indicate that the tetrafluorohydroquinone ring of the macrocyclic polyether cannot reside inside the cavity of the tetracationic cyclophane in the [2]catenane **7**·4PF$_6$.

[20] The tetracationic cyclophane displays characteristic twisting (outside, 2°, inside, 2°) and bowing (outside, 26°, inside 25°) distortions with the bipyridinium units.

[21] Amabilino, D. B.; Ashton, P. R.; Stoddart, J. F.; Tolley, M. S.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1297−1301.

[22] The author has deposited atomic coordinates for **4** and **7**·4PF$_6$ with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.